2-methylbutyryl-CoA dehydrogenase deficiency

2-methylbutyryl-CoA dehydrogenase deficiency is a rare disorder in which the body is unable to process proteins properly. Normally, the body breaks down proteins from food into smaller parts called amino acids. Amino acids can be further processed to provide energy for the body. People with 2-methylbutyryl-CoA dehydrogenase deficiency cannot process a particular amino acid called isoleucine.

Most cases of 2-methylbutyryl-CoA dehydrogenase deficiency are detected shortly after birth by newborn screening, which identifies abnormal levels of certain compounds in the blood. In individuals with this condition, a compound called 2-methylbutyryl carnitine is elevated in the blood and another called 2-methylbutyrylglycine is elevated in the urine (2-methylbutyrylglycinuria).

Most people with 2-methylbutyryl-CoA dehydrogenase deficiency have no health problems related to the disorder. A small percentage of affected individuals develop signs and symptoms of the condition, which can begin soon after birth or later in childhood. The initial symptoms often include poor feeding, lack of energy (lethargy), vomiting, and irritability. These symptoms sometimes progress to serious health problems such as difficulty breathing, seizures, and coma. Additional problems can include poor growth, vision impairment, learning disabilities, muscle weakness, and delays in motor skills such as standing and walking.

It is unclear why some people with 2-methylbutyryl-CoA dehydrogenase deficiency develop health problems and others do not. Doctors suggest that in some cases, signs and symptoms may be triggered by infections, prolonged periods without food (fasting), or an increased amount of protein-rich foods in the diet.

Frequency

2-methylbutyryl-CoA dehydrogenase deficiency is a rare condition; its worldwide prevalence is unknown. This condition is most common among Hmong populations in Southeast Asia and in people of Hmong descent, affecting 1 in 250 to 1 in 500 people in these communities. These individuals do not usually develop health problems related to the condition.

Genetic Changes

Mutations in the *ACADSB* gene cause 2-methylbutyryl-CoA dehydrogenase deficiency. This gene provides instructions for making an enzyme called 2-methylbutyryl-CoA dehydrogenase, which performs a chemical reaction that helps process the amino acid isoleucine. Mutations in the *ACADSB* gene reduce or eliminate the activity of this enzyme. With a shortage (deficiency) of 2-methylbutyryl-CoA dehydrogenase activity,

the body is unable to break down isoleucine properly. Researchers speculate that some features of this disorder, such as lethargy and muscle weakness, occur because isoleucine is not converted to energy. In addition, impairment of 2-methylbutyryl-CoA dehydrogenase may allow the buildup of toxic compounds, which can lead to serious health problems.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 2-MBADD
- 2-MBCD deficiency
- 2-MBG
- 2-methylbutyryl-coenzyme A dehydrogenase deficiency
- 2-methylbutyryl glycinuria
- SBCADD
- short/branched-chain acyl-CoA dehydrogenase deficiency

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Elevated C5 Acylcarnitine
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C5.pdf

Genetic Testing

- Genetic Testing Registry: Deficiency of 2-methylbutyryl-CoA dehydrogenase
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1864912/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/2-methylbutyrylglycinuria

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Amino Acid Metabolism Disorders
  https://medlineplus.gov/aminoacidmetabolismdisorders.html
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- 2-methylbutyryl-CoA dehydrogenase deficiency
  https://rarediseases.info.nih.gov/diseases/10322/2-methylbutyryl-coa-dehydrogenase-deficiency

Educational Resources

- Disease InfoSearch: 2-Methylbutyryl-CoA Dehydrogenase Deficiency
  http://www.diseaseinfosearch.org/2-Methylbutyryl-CoA+Dehydrogenase+Deficiency/18
- MalaCards: 2-methylbutyryl-coa dehydrogenase deficiency
  http://www.malacards.org/card/2_methylbutyryl_coa_dehydrogenase_deficiency
- Monroe Carell Jr. Children's Hospital at Vanderbilt
  http://www.childrenshospital.vanderbilt.org/uploads/documents/mg_pt.organic_acidemias.pdf
- Orphanet: 2-methylbutyryl-CoA dehydrogenase deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=79157

- Screening, Technology, and Research in Genetics
  http://www.newbornscreening.info/Parents/organicaciddisorders/2MBC.html
- Waisman Center
  http://www.waisman.wisc.edu/2mbadd/general.html

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB)
  http://www.climb.org.uk/
- Organic Acidemia Association
  http://www.oaanews.org/2mbcd.html

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%282-methylbutyryl-coenzyme+A+dehydrogenase+deficiency%29+OR+%282-methylbutyrylglycine%5BTIAB%5D%29+OR+%28sbcadd%5BTIAB%5D%29+OR+%28short/branched-chain+acyl-coa+dehydrogenase+deficiency%29+OR+%282-MBG%5BTIAB%5D%29+OR+%282-MBCDase%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- 2-METHYLBUTYRYL-CoA DEHYDROGENASE DEFICIENCY
  http://omim.org/entry/610006

Sources for This Summary

- Alfardan J, Mohsen AW, Copeland S, Ellison J, Keppen-Davis L, Rohrbach M, Powell BR, Gillis J, Matern D, Kant J, Vockley J. Characterization of new ACADSB gene sequence mutations and clinical implications in patients with 2-methylbutyrylglycinuria identified by newborn screening. Mol Genet Metab. 2010 Aug;100(4):333-8. doi: 10.1016/j.ymgme.2010.04.014.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20547083
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2906669/
- Andresen BS, Christensen E, Corydon TJ, Bross P, Pilgaard B, Wanders RJ, Ruiter JP, Simonsen H, Winter V, Knudsen I, Schroeder LD, Gregersen N, Skovby F. Isolated 2-methylbutyrylglycinuria caused by short/branched-chain acyl-CoA dehydrogenase deficiency: identification of a new enzyme defect, resolution of its molecular basis, and evidence for distinct acyl-CoA dehydrogenases in isoleucine and valine metabolism. Am J Hum Genet. 2000 Nov;67(5):1095-103. Epub 2000 Sep 29.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11013134
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1288551/
- Korman SH. Inborn errors of isoleucine degradation: a review. Mol Genet Metab. 2006 Dec;89(4): 289-99. Epub 2006 Sep 6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16950638

- Madsen PP, Kibaek M, Roca X, Sachidanandam R, Krainer AR, Christensen E, Steiner RD, Gibson KM, Corydon TJ, Knudsen I, Wanders RJ, Ruiter JP, Gregersen N, Andresen BS. Short/branched-chain acyl-CoA dehydrogenase deficiency due to an IVS3+3A>G mutation that causes exon skipping. Hum Genet. 2006 Feb;118(6):680-90. Epub 2005 Nov 30.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16317551
- Matern D, He M, Berry SA, Rinaldo P, Whitley CB, Madsen PP, van Calcar SC, Lussky RC, Andresen BS, Wolff JA, Vockley J. Prospective diagnosis of 2-methylbutyryl-CoA dehydrogenase deficiency in the Hmong population by newborn screening using tandem mass spectrometry. Pediatrics. 2003 Jul;112(1 Pt 1):74-8. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12837870
- Pasquali M, Monsen G, Richardson L, Alston M, Longo N. Biochemical findings in common inborn errors of metabolism. Am J Med Genet C Semin Med Genet. 2006 May 15;142C(2):64-76. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16602099
- Sass JO, Ensenauer R, Röschinger W, Reich H, Steuerwald U, Schirrmacher O, Engel K, Häberle J, Andresen BS, Mégarbané A, Lehnert W, Zschocke J. 2-Methylbutyryl-coenzyme A dehydrogenase deficiency: functional and molecular studies on a defect in isoleucine catabolism. Mol Genet Metab. 2008 Jan;93(1):30-5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17945527

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/2-methylbutyryl-coa-dehydrogenase-deficiency

Reviewed: February 2017
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services